Introduction
Dr. Pavol Cekan believes that RNA-based techniques hold the secret to creating reliable, 100% accurate, quantitative and affordable diagnostics for cancer. In this exclusive interview, he describes how this approach could revolutionize cancer treatment, making it possible to precisely determine cancer type and decide on the right medical approach.
“We believe there is so much that can be improved in diagnostics to unlock the full potential of personalized medicine”

— Dr. Pavol Cekan, CEO of MultiplexDX

Dr. Pavol Cekan studied biochemistry and synthetic chemistry at the University of Iceland in Reykjavik, focusing on the structure and function of nucleic acids, especially RNA. He finished his PhD with 18 publications in his field, and was successful in his application to Professor Thomas Tuschl's lab in 2009. Dr. Cekan's work with this pioneer in RNA biology focused on RNA fluorescence in situ hybridization (FISH), designing on a new fixation method for tissues and cells that would retain small RNA (e.g., miRNA, piRNA), new probes that are specific for any RNA, and multicolor FISH techniques for multiplex analyses.

This complete reinvention of RNA FISH technology led to very significant projects focused on the modeling and discrimination of tumor types, specifically basal cell carcinoma and Merkel cell carcinoma (1, 2). The techniques developed enabled the first 100% successful discrimination of the two skin tumor types, which have overlapping histologic features but distinct cellular origins. As Merkel cell carcinoma is an aggressive cancer that is quick to metastasize, its successful early identification is a significant step forward in cancer diagnostics. The techniques are also being applied to breast cancer discrimination.

While with Professor Tushl's group, Dr. Cekan developed 8-color RNA FISH techniques, collaborating with Perkin Elmer on their first implementation. This led to the successful simultaneous visualization of 8 RNAs for the first time. It is another major development in the direction of rapid RNA-based diagnostics.

Having seen the success of these techniques, Dr. Cekan began to consider their broader applications in personalized molecular diagnostics, especially in the elimination of cancer misdiagnosis. After three years at the National Cancer Institute studying the cell cycle, DNA damage response and repair mechanisms, cell senescence and cell models of cancer (3), he saw the potential of a company focused on applying RNA FISH and RNA sequencing to patient care.

Together with his friend and fellow molecular biologist, Dr. Vladimir Wolf, he founded MultiplexDX, with the mission to create reliable, 100% accurate, quantitative and affordable diagnostics for cancer. He met with Elsevier to discuss how the work at MultiplexDX opens new possibilities in the quest for truly personalized medicine.
How did you identify the niche for MultiplexDX?

We decided to found MultiplexDX when we realized that RNA FISH and RNA sequencing have enormous potential for accurate diagnoses. Every cancer is unique. Every patient deserves a personalized diagnosis that can actually indicate the therapy that they really need.

When I was working on my last project in Professor Tuschl’s lab—the discrimination of breast cancer types—I did a lot of research into current diagnostic techniques and I began to see how many of them fall short. When people get sick, they go to a doctor and they undergo what are often quite old-fashioned tests based on techniques like histology and immunohistochemistry. This can lead to misdiagnoses, which means being put on therapy that is completely wrong for the actual underlying condition. Even if the diagnosis is close to being correct, the patient might be on the wrong dosage or the length of therapy is too long or not long enough. The physicians monitor the response to the therapy and only if it doesn’t work do they consider something different. In the case of aggressive cancers, the patient might not have the time to wait for monitor–response approaches to reveal what’s going on.

Why are the RNA-based technologies that were successfully applied in your studies not in wider clinical use?

They are widely used, but not by the medical industry. More precise, more accurate molecular diagnostic techniques are common in academia, but they haven’t found the same acceptance in clinical settings.

It’s a financial consideration. The big profit is still thought to lie in pharmaceutical development. Diagnostics doesn’t seem profitable so there’s very little investment in changing or replacing the old-fashioned approaches.

How is MultiplexDX able to invest in these techniques?

One of the advantages of a startup is the size, which equates with a smaller need for investment. This gives them the agility to be innovative and try things that a larger company would not be able to justify financially.

We’ve been able to get the small amount of financing to prove our concept and now we can use that proof to look for more investment to further develop the technology. We’re developing a revolutionary Multiplex+ technology combining multiplex RNA sequencing and multi-color RNA visualization. Our agile startup business model has left us open to many different possibilities for creating applications.
And your goal is to create personalized diagnostics for a whole range of cancers.

To be more precise, we believe that we can create a system that will use RNA information and 100% accurate quantification to generate a specific barcode for each cancer that not only identifies it accurately but also indicates what treatment is right: the drug, the dose, the duration. The potential is there.

Does your diagnostic methodology have the potential to feed back into the pharmaceutical industry and inform drug development?

The main information that we could contribute to early drug development would be identifying the lack of a treatment. Since our goal is 100% accurate personalized diagnosis, we’re essentially focused on supporting clinical decisions. However, if we identified the cancer but also saw that there is no existing treatment for it, then that information could feed back into early drug development, whether it’s the development of a new drug or the repurposing of an existing one.

When you consider how many drugs exist on the market or are in clinical trials, it seems that there are more than enough to work with. In 10 years, there will probably be more than 1,000 anti-cancer drugs. I am not sure that we would need more drugs—but we do need better diagnostics to enable us to work with what we have, and to enable the patient’s point of entry to treatment to be a successful one.

Would your techniques also help with response monitoring or testing drugs in clinical trials?

Absolutely. Visualizing what occurs at the RNA level and what is happening with other biomarkers—this is a dynamic technique. As treatment progresses, we could use fluorescence sensors to monitor for reporters for apoptosis to see if cells are dying and what type. You could look at the RNA at each stage of the cell cycle to see what the cell is doing, where it is arresting or progressing through the stages of the cell cycle, whether on its own or in response to a drug.

Some of this is still theory. We are still developing the techniques and other labs are also looking at different ways to examine the whole transcriptome. What is important is that the potential is definitely there and with the right investment, we could push the envelope to be able to not only diagnose cancer accurately, but also accurately visualize the effects of a drug in vivo.
What is next for MultiplexDX?
We will continue to look at RNA, including extracellular RNA and continue to develop and validate novel products and kits for RNA library preparation and RNA visualization.

When a cancer cell releases DNA through exosomes or cell death, it also releases RNA. You can get a bigger picture from RNA. We’re also looking at blood tests for ctRNA to investigate the potential of annual transcriptomics in the early diagnosis of cancer.

We believe there is so much that can be improved in diagnostics to unlock the full potential of personalized medicine and it is a privilege to be at the forefront of that.

To learn more about MultiplexDX, please visit multiplexdx.com.

REFERENCES


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